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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,935	05/03/2001	David F. Woodward	D2914	6555

33197 7590 05/17/2007

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EXAMINER	
FUBARA, BLESSING M	

ART UNIT	PAPER NUMBER
1618	

MAIL DATE	DELIVERY MODE
05/17/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

TJA

Office Action Summary	Application No.	Applicant(s)	
	09/847,935	WOODWARD ET AL.	
	Examiner	Art Unit	
	Blessing M. Fubara	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 2/28/07.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 60-66,68,72,73,77 and 87-90 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 60-66,68,72,73,77 and 87-90 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of amendment and remarks filed 2/28/07. Claims 60-66, 68, 72, 73, 77 and 87-90 are pending.

Previous rejections that are not reiterated herein are withdrawn

The Invention:

The rejections below are based on applicants' claim (claim 60) to composition comprising ion-pair complex comprising a therapeutic component that is adrenergic agonist, efficacy enhancing component and a carrier component, which includes saline. The efficacy enhancing component is selected form fatty acid, anionic polymers and mixtures thereof. The efficacy enhancing component "being effective to enhance the movement of the therapeutic component across a lipid membrane, or biological membrane under physiological conditions" is a property/function of the efficacy enhancing component and a property/function of a product/material or the efficacy enhancing agents is an inherent feature of the product/material or efficacy enhancing component. An ion-pair complex forms between pairs of ions having opposite charge. As is taught in applicants' specification at paragraph 77 of the published application, a complex forms when efficacy-enhancing component is added to a solution containing a therapeutic agent. Thus a solution containing therapeutic component and efficacy enhancing component would have complex formed between the efficacy enhancing component and the therapeutic component.

In claim 87, the efficacy-enhancing component in is selected form fatty acid, anionic polymers and mixtures thereof. "Effective to enhance movement of the therapeutic component across a lipid membrane, or a biological membrane ...efficacy enhancing component" is a

property of the composition. Efficacy enhancing component that is "present in an amount sufficient to complex substantially all of the therapeutic component in solution" is any amount and the claims have not recited any amount. As it regards the recitation that a molar ratio of therapeutic component to efficacy enhancing component, it is noted that interactions or combinations or combinations takes place in molar proportions. According to MPEP 2112.01 [R-3] II, *"products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990.).*

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 87 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by DeSantis, Jr. et al. (US 5,811,443).

DeSantis discloses combination of at least one clonidine derivative, which is an alpha-2-adrenergic agonist, at least one prostaglandin (abstract; column 2, lines 25-37); the composition may additionally contain anionic mucomimetic polymers in amounts of between about 0.05 and

about 8.0 wt% and specifically pourable liquid formulations contain between about 0.05 and 2.0 wt % (column 8, lines 57-64) of the anionic polymers; the composition further comprises agents for adjusting tonicity and osmolality and those agents include sodium chloride, potassium chloride, mannitol, dextrose, glycerine and propylene glycol (column 8, lines 32-36) and the tonicity agents are used in amounts of between about 0.1 to about 10.0 wt% (column 8, lines 36-38). The composition is aqueous and has pH of between 3.5 and 8.0 and osmolality of between 280 to 320 milliOsmoles per kilogram (column 9, lines 35-37).

Prostaglandin is physiologically active compound derived from fatty acid. Prostaglandin is present at amounts of 0.00001 to 0.2 wt% (column 8, lines 7 and 8; claim 12); prostaglandin is a complex fatty acid as described in the as filed specification at page 13, second full paragraph. The anionic polymer and prostaglandin are efficacy-enhancing components. DeSantis discloses that the ratio of prostaglandin to clonidine is 1:1 to 1:10,000 (column 8, lines 14-17). Since 1 mole of Ca^{2+} combines with 1 mole of SO_4^{2-}, and 2 moles of Cl^- combine with 1 mole of Ca^{2+}, it flows that depending on the pH of the medium, ionic efficacy enhancing component and ionic therapeutic agent will combine in molar proportions so that the molar ratios recited in the claims are inherent to specific therapeutic component-efficacy enhancing component pair, which thus meets the limitation of claim 87. In this case, no specific therapeutic agent is claimed and no specific efficacy-enhancing component is claimed. A solution of sodium chloride and water is saline and meets the limitation of saline in claim 1. Since according the applicants' specification at paragraph [0077] of the published application, a complex forms between the therapeutic component and the efficacy-enhancing component in solution, it is plausible that a

complex is formed between the clonidine, which is the therapeutic component and the anionic polymer, which is the efficacy-enhancing component.

Clonidine is alpha-2-adrenergic agonist meeting the limitation of claims 88. Therefore, DeSantis meets the limitations of the designated claims.

3. Claims 87, 88 and 90 are rejected under 35 U.S.C. 102(e) as being anticipated by Beck et al. (US 6,358,935).

Beck discloses composition comprising brimonidine (0.2% w/v), sodium carboxymethylcellulose (0.5%) and cyclodextrin (present in Example 2); the composition is at pH of 7.4 (Examples 1 and 2) and in saline (column 6, line 59). pH of 7.4 is greater than 7 and lies between the recited pH of 7-9 (claims 65 and 66). Specifically, Beck discloses the formation of complex between cyclodextrin and the therapeutic agent (column 6, lines 18-40). Beck envisions the molar ratio of cyclodextrin to active agent in the range of 10:1 to about 1:1 or less and preferably at about 5:1 to about 1:1 or less and points within this disclosed ratio touch the recited ratio. The carboxymethylcellulose meets the limitation of an additional efficacy-enhancing component of claim 77. The ratio of the therapeutic agent quinoxaline to the cellulose is 1:1 in example 1.

4. Claims 60-62, 64, 68, 87 and 88 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Uehara et al. (JP 11-130656, computer translated document).

Uehara teaches composition comprising ω-3 based polyunsaturated fatty acid and/or its derivatives such as eicosapentaenoic acid, docosahexaenoic acid and a-linolenic acid at 0.0001-

10 wt%, caffeine or theophyline or β-adrenergic stimulant and/or α-2 adrenergic inhibitor (abstract). The combination of β-adrenergic stimulant and α-2 adrenergic inhibitor meet the requirements of claim 64. The discloses 5 amount of the fatty acid at 0.0001-10 wt% meet the amount of the fatty acid in claim 60. The α-2 adrenergic meets claims 61, 62 and 88. Ophthalmically acceptable in claim 68 is the characteristic/property of the composition and the composition of Uehara is capable of ophthalmic use. Since 1 mole of Ca^{2+} combines with 1 mole of SO_4^{2-}, and 2 moles of Cl^- combine with 1 mole of Ca^{2+}, it flows that depending on the pH of the medium, ionic efficacy enhancing component and ionic therapeutic agent will combine in molar proportions so that the molar ratios recited in the claims are inherent to specific therapeutic component-efficacy enhancing component pair, which thus meets the limitation of claim 87. Uehara thus meets the claims and in the alternate, the recited molar ratios would be obvious because compounds combine in whole number ratios based on the molar relationships of the combining parts.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 89 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beck et al. (US 6,358,935).

Beck is described above. Beck does not disclose the quinoxaline of claim 89. One quinoxaline can be substituted for another and expect to obtain the same effect. Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teaching of Beck where the composition comprises methylcellulose and/or cyclodextrin and substitute 2-imidazolin-2-ylamino) quinoxaline for brimonidine tartrate with the expectation that the composition would produce the same effect in when administered to the eye.

8. Claims 60-63, 65, 66, 68, 72, 73, 77 and 87-90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gil et al. (US 6,294,553).

Gil discloses a composition that comprises brimonidine, which is a 5-bromo-6 (2-imidazolin-2-ylamino) quinoxaline and an alpha-2-agonist (abstract, column 2, lines 50 and 61; column 3, lines 12, and 37-39), oleic acid or anionic surfactant (column 4, lines 20-22), buffers (column 4, lines 28-37), physiological saline solution and vehicles such as poloxamers and

cellulose polymers (column 4, lines 4-10); the composition of Gil is applicable as an ophthalmic with a physiological saline solution as the vehicle and where the pH of the ophthalmic composition is between 6.5 and 7.2 (column 3, lines 65-67). Oleic acid is a fatty acid. Effective amount is any amount. A pH of 7.2 is greater than 7 and lies between 7 and 9 (claims 65 and 66) meeting claims 64 and 65. Oleic acid, a fatty acid and anionic polymers are efficacy-enhancing components meeting the requirements of claims 60 and 87. While claim 68 recites the property/characteristic of the claimed composition, Gill also teaches that the composition is applicable as an ophthalmic composition, thus meeting claim 68. The brimonidine meets the requirements of claims 60-63 and 87-90. Since 1 mole of Ca^{2+} combines with 1 mole of SO_4^{2-}, and 2 moles of Cl^- combine with 1 mole of Ca^{2+}, it flows that depending on the pH of the medium, ionic efficacy enhancing component and ionic therapeutic agent will combine in molar proportions so that the molar ratios recited in the claims are inherent to specific therapeutic component-efficacy enhancing component pair, which thus meets the molar ratio requirements of claims 60 and 87. Also, regarding the molar ratios, there is no demonstration that the cited ratios provided unexpected and unusual results.

Gill does not disclose the amount of the efficacy-enhancing component. Also, since Gill is silent on the amount of the efficacy-enhancing component, it would appear that all or certain amount of the efficacy-enhancing component would be suitable to provide the desired composition and effect and it is within the purview of the person of skill or of ordinary skill to determine the workable amount of the efficacy-enhancing component. The burden is on applicant to demonstrate that the recited amounts provide unexpected result.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the quinoxaline composition according to Gill. One having ordinary skill in the art at the time the invention was made to use amount of efficacy enhancing component effective for ocular composition. And, differences in concentration/amounts will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration/amount is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Secondly, there is no demonstration in applicants' specification showing that efficacy enhancing component in amounts greater than 0.2% and less than 10% provides unusual results.

"When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Blessing M. Fubara whose telephone number is (571) 272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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